

fusion peptide. The claims of Group III relates to cells which express the fusion peptide. They do so because they contain a recombinant polynucleotide of the type described in Claim 1.

The Examiner rejected claims 1-7 under 35 USC § 112, second paragraph, as being indefinite. The Examiner asserts that claim 1 is unclear because it is not clear whether the protein comprises A, C and D, with another polypeptide chain B linked to A, by disulfide bonds, for example, or whether the polynucleotide encodes all of the recited parts A, B, C and D. Applicants point out that claim 1 recites a polynucleotide encoding a fusion protein. The Examiner has not provided any evidence or argument as to why a person skilled in the art would consider that this term encompassed multimers or peptides associated by disulfide bonds. Nevertheless, to avoid any conceivable ambiguity, Applicants have amended claim 1 to unequivocally establish that all of the recited parts of the peptide are parts of a fusion protein for which the polynucleotide codes.

Claim 2 has been corrected to correct the typographical error noted by the Examiner.

With respect to claims 3 and 6, the Examiner asserts that the meaning of the term "suicide gene" is unclear, and then proceeds to acknowledge the meaning of the term. In the circumstances, the Examiner has plainly not established that a person skilled in the art would have any trouble understanding the meaning of this term. Furthermore, it is noted that the term "suicide gene" is well understood in the art and requires no further explication than that which is provided. For example, US Patent No. 5,674,486 states that:

Suicide genes can be incorporated into the CE cells or carrier cells to allow for selective inducible killing after stimulation of the immune response. A gene such as the herpes simplex virus thymidine kinase gene (TK) can be used to create an inducible destruction of the CE cells or carrier cells. When the CE cells or carrier cells are no longer useful, a drug such as acyclovir or gancyclovir can be administered. Either of these drugs will selectively kill cells expressing TK, thus eliminating the implanted transduced cells.

Similarly, the background section of US Patent No. 5,856,153

One strategy for the treatment of localized disease is to render targeted cells sensitive to normally nontoxic chemotherapeutic agents using so-called "suicide genes" such as the herpes simplex virus thymidine kinase (HSV-tk) gene, the related varicella zoster TK gene or the bacterial xanthine/guanine phosphoribosyltransferase gpt gene. HSV-tk, for example, converts the nontoxic guanosine analogue ganciclovir into a phosphorylated compound that acts as a

chain terminator in DNA synthesis, selectively killing dividing cells.

Both of these patents were filed well before the present application, and thus are fairly representative of knowledge in the art when this application was filed.

Claims 4 and 6 have been amended in view of the Examiner's remarks about a polynucleotide not encoding a gene and now recite that the polynucleotide comprises a suicide gene. Applicants respectfully traverse the Examiner's rejection to the extent it makes the argument that a polynucleotide cannot encode a gene, and that a person skilled in the art would have any trouble understanding the scope of claims 4-6 as amended. The Examiner states that

From the teachings of the specification, however, the "suicide gene" is not defined.

This is in error, since specific examples of well known and art recognized suicide genes, namely thymidine kinase or bacterial cytosine deaminase are provided. The Examiner further states that

[the suicide gene] appears not to be limited to the specific coding regions, and include expression control elements that fall under the definition of gene.

This statement is very difficult to understand. Is the Examiner saying that the suicide gene is not a gene because it includes expression control elements or because it does not? In either case, Applicants enquire as to the portions of the specification on which the Examiner is relying for support for the assertion. Finally, Applicants respectfully submit that the Examiner has not explained why a person skilled in the art would have trouble understanding the scope of the claims. The polynucleotide includes bases, such that when the polynucleotide is expressed, one of the expression products is a protein such as thymidine kinase which makes the susceptible to a specific cytotoxic agent. This makes it possible for one to cause the cells expressing the polynucleotide to be killed selectively because they express the polynucleotide. This is the art understood meaning of a suicide gene, and there is no lack of clarity in the claims. Thus, the rejection of claims 1-7 under 35 USC § 112, second paragraph, should be withdrawn.

The Examiner also rejected claims 1-7 under 35 USC § 112, first paragraph, as lacking enablement. Claim 1 has been amended in view of the Examiner's remarks. These amendment are supported, *inter alia*, in Fig. 1. With respect to the suicide gene, however, the Examiner has failed to provide any reasoning why the positioning of this portion of the DNA is critical, given the fact that it produces a separate protein. Furthermore, Applicants would point out that it is the specification, not the claims which teaches how to make and use the invention.

Claims need not be drafted in sufficient details to provide an enabling disclosure on their own, nor need they include limitations sufficient to exclude things that would be obviously inoperative to persons skilled in the art. Accordingly, Applicants submit that claims 1-7, as amended, are in full compliance with the requirements of 35 USC § 112, first paragraph.

The Examiner also rejected claims 1-7 asserting that there was a lack of written description for the invention as a whole, because the claims encompass suicide genes, but there are variants of the species disclosed and species of suicide genes not disclosed, such that Applicants have not shown they had possession of the full scope of the invention. Applicants respectfully submit that this is an improper application of the written description requirement of 35 USC § 112 first paragraph. Indeed, if this argument were correct, then no claim which included the open-ended term “comprising” would ever meet the written description requirement. For example, a claim to a car that uses the word “comprising” would encompass a car with a rhinoceros bolted to the hood. This does not mean that the specification must include a discussion of how to bolt on the rhinoceros, or of how to make the hood strong enough to support its weight in order to have a written description of the invention. In the circumstances, the written description rejection under 35 USC § 112, first paragraph should be withdrawn.

The Examiner has provisionally rejected claims 1-7 under the judicially-created doctrine of double patenting in view of commonly assigned copending application no. 09/142,974 in view of several secondary references. Applicants will address this rejection, if it maintained, at such time as claims are allowed in both of the application, and reserve the right to address whether or not the secondary references are in fact available as art for such a rejection.

The Examiner rejected claims 1-2 as anticipated by Alvarez-Vallina. Applicants note that the Examiner has cited this paper as art under 35 USC § 102(b), but has not provided any evidence as to actual date of publication. It is respectfully submitted that this reference is at best art under 35 USC § 102(a), which Applicants are entitled to antedate if able. At present, material is being collected for submission of a Declaration Under Rule 131 for this purpose. Similarly, this declaration will plainly remove Cheung et al (WO97/34634) which was published a mere 5 days before the filing of this application as a reference. Thus, the rejections under 35 USC § 103 will also be obviated by this submission. Nevertheless, it is noted that in making the rejections under 35 USC § 103, the Examiner has failed to apply the same standards that he

applied in the remainder of the Office Action. For example, much of the office action is predicated upon an asserted unpredictability in the art, yet no such unpredictability is taken into account when the rejection for obviousness is made. Indeed, he has not addressed the basis for an expectation of success, beyond taking one summarizing sentence from the introduction of Alvarez-Vallina, which could as easily be read as saying they show one example and offering a prediction that any and all scFV will work in their model. Applicants respectfully submit that a uniform standard must be applied reflecting a single level of skill in the art, and that it is unfair and improper to use a very low level of skill when considering enablement and a very high level of skill when considering obviousness.

Respectfully submitted,

A handwritten signature in cursive script, reading "Marina T. Larson", with a long horizontal flourish extending to the right.

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